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Claims

1. A method for diagnosing or prognosing Alzheimer's disease in a subject, or determining whether a subject is at increased risk of developing Alzheimer's disease, comprising:

   determining a level, or an activity, or both said level and said activity, of a transcription product and/or a transiation product of (i) a cystatin C gene or (ii) a polymorphic variant of a cystatin C gene in a sample from said subject;

   and

   comparing said level, or said activity, or both said level and said activity, of said transcription product and/or said translation product to a reference value representing a known disease or health status, whereby an increase of a level or a varied activity of a translation product of (i) a cystatin C gene or (ii) a polymorphic variant of a cystatin C gene in said cerebrospinal fluid from said subject relative to a reference value representing a known health status indicates a diagnosis, or prognosis, or increased risk of Alzheimer's disease in said subject.

2. A method of monitoring the progression of Alzheimer's disease in a subject, comprising:

   determining a level, or an activity, or both said level and said activity, of a transcription product and/or a translation product of (i) a cystatin C gene or (ii) a polymorphic variant of a cystatin C gene in a sample from said subject;

   and

   comparing said level, or said activity, or both said level and said activity, of said transcription product and/or said translation product to a reference value representing a known disease or health status,

thereby monitoring the progression of Alzheimer's disease in said subject.

3. A method of evaluating a treatment for Alzheimer's disease, comprising:

determining a level, or an activity, or both said level and said activity, of a transcription product and/or a translation product of (i) a cystatin C gene or (ii) a polymorphic variant of a cystatin C gene in a sample obtained from a subject being treated for Alzheimer's disease;

and

comparing said level, or said activity, or both said level and said activity, of said transcription product and/or said translation product to a reference value representing a known disease or health status,

thereby evaluating said treatment for Alzheimer's disease.

4. The method according to one of claims 1 to 3, wherein said sample is a body fluid, preferably cerebrospinal fluid.

5. The method according to one of claims 1 to 4, wherein said subject is a human.

6. The method according to one of claims 1 to 5, wherein said translation product of (i) a cystatin C gene or (ii) a polymorphic variant of a cystatin C gene is determined in its monomer form.

7. The method according to one of claims 1 to 6, wherein said translation product and/or said transcription product is detected using an immunoassay, an enzyme activity assay and/or a binding assay.

8. The method according to one of claims 1 to 7, wherein said reference value is that of a level, or an activity, or both said level and said activity, of a transcription product and/or a translation product of (i) a cystatin C gene or (ii) a polymorphic variant of a cystatin C gene in a sample from a subject not suffering from said Alzheimer's disease.

9. The method according to one of claims 1 to 8, further comprising comparing a level, or an activity, or both said level and said activity, of a transcription product and/or a translation product of (i) a cystatin C gene or (ii) a polymorphic variant of a cystatin C gene, in said sample with a level, an activity, or both said level and said activity, of a transcription product and/or a translation product of (i) a cystatin C gene or (ii) a polymorphic variant of a cystatin C gene in a series of samples taken from said subject over a period of time.

10. The method according to claim 9, wherein said subject receives a treatment prior to one or more sample gatherings.

11. The method of claim 10, wherein said level, or said activity, or both said level and said activity, in said samples is determined, before and after said treatment of said subject.

12. A method of diagnosing or prognosing Alzheimer's disease in a subject, or determining whether a subject is at increased risk of developing Alzheimer's disease comprising:

determining a presence or absence of a polymorphism in a cystatin C gene in a sample from said subject,

thereby diagnosing or prognosing Alzheimer's disease in said subject, or determining whether said subject is at increased risk of developing Alzheimer's disease.

13. The method of claim 12, wherein a presence of a polymorphism in leucin 68 codon of a human cystatin C gene leading to a loss of *Alu* I restriction site does not indicate diagnosis, or prognosis, or increased risk of Alzheimer's disease in said subject.

14. The method of claim 12 and/or 13, wherein the presence or absence of at least one B allele is determined.

15. The method of claim 14, wherein the presence of at least one B allele, in particular the presence of the B/B genotype, indicates said subject is at increased risk of developing Alzheimer's disease or indicates a diagnosis or prognosis of Alzheimer's disease.

16. The method of at least one of claims 12 to 15, further comprising:

determining a level, or an activity, or both said level and said activity, of a transcription product and/or a translation product of (i) a cystatin C gene or (ii) a polymorphic variant of a cystatin C gene in a sample from said subject;

and

comparing said level, or said activity, or both said level and said activity, of said transcription product and/or said translation product to a reference value representing a known disease or health status.

17. Use of a kit for the diagnosis, or prognosis, or determination of increased risk of developing Alzheimer's disease, or monitoring a progression, or monitoring success or failure of a therapeutic treatment of Alzheimer's disease in a subject, said kit comprising:

(a) at least one reagent which is selected from the group consisting of

- reagents that selectively detect a transcription product of (i) a cystatin C gene or (ii) a polymorphic variant of a cystatin C gene,
- reagents that selectively detect a translation product of (i) a cystatin C gene or (ii) a polymorphic variant of a cystatin C gene, and
- reagents that selectively detect the presence or absence of a polymorphism in a cystatin C gene; and

(b) instructions for diagnosing, or prognosing, or determining increased risk of developing Alzheimer's disease, or monitoring a progression, or monitoring success or failure of a therapeutic treatment of Alzheimer's disease in a subject by

- detecting a level, or an activity, or both said level and said activity, of said transcription product and/or said translation product of (i) a cystatin C gene or (ii) a polymorphic variant of a cystatin C gene, in a sample from said subject; and/or detecting a presence or absence of a polymorphism in said cystatin C gene in a sample from said subject; and

- diagnosing, or prognosing, or determining whether said subject is at increased risk of developing Alzheimer's disease, wherein a varied level, or activity, or both said level and said activity, of said transcription product compared to a reference value representing a known health status; or an increase of a level or a varied activity of said translation product of (i) a cystatin C gene or (ii) a polymorphic variant of a cystatin C gene relative to a reference value representing a known health status; or a level, or activity, or both said level and said activity, of said transcription product and/or said translation product similar or equal to a reference value representing a known disease status; or the presence of a polymorphism in said cystatin C gene indicates a diagnosis, or prognosis, or increased risk of developing Alzheimer's disease.

18. Use according to claim 17, wherein a presence of a polymorphism in leucin 68 codon of a human cystatin C gene leading to a loss of *Alu* I restriction site does not indicate diagnosis or prognosis of Alzheimer's disease in said subject.

19. Use according to one of claims 17 and/or 18, further comprising reagents to assess a function or dysfunction of said subject's kidneys.

20. Use according to one of claims 17 to 19, wherein said translation product of (i) a cystatin C gene or (ii) a polymorphic variant of a cystatin C gene is determined in its monomer form.

21. Use according to at least one of claims 17 to 20 for use in monitoring a progression of Alzheimer's disease in a subject.

22. Use according to at least one of claims 17 to 20 for use in monitoring success or failure of a therapeutic treatment of said subject.

23. A kit for the diagnosis or prognosis, or determination of increased risk of developing Alzheimer's disease in a subject, said kit comprising:

(a) reagents that selectively detect the presence or absence of a polymorphism in a cystatin C gene; and

(b) instructions for diagnosing, or prognosing, or determining increased risk of developing Alzheimer's disease in a subject by

- determining the presence or absence of a polymorphism in a cystatin C gene; and

- diagnosing, or prognosing, or determining whether said subject is at increased risk of developing Alzheimer's disease, wherein

the presence of at least one B allele, in particular the presence of the B/B genotype, indicates a diagnosis, or prognosis, or an increased risk of developing Alzheimer's disease

24. The kit according to claim 23, further comprising

(a) reagents that selectively detect a transcription product of (i) a cystatin C gene or (ii) a polymorphic variant of a cystatin C gene,

reagents that selectively detect a translation product of (i) a cystatin C gene or (ii) a polymorphic variant of a cystatin C gene, and

(b) instructions for diagnosing, or prognosing, or determining increased risk of developing Alzheimer's disease in a subject by

- detecting a level, or an activity, or both said level and said activity, of said transcription product and/or said translation product of (i) a cystatin C gene or (ii) a polymorphic variant of a cystatin C gene, in a sample from said subject; and

- diagnosing, or prognosing, or determining whether said subject is at increased risk of developing Alzheimer's disease, wherein a varied level, or activity, or both said level and said activity, of said transcription product compared to a reference value representing a known health status; or an increase of a level or a varied activity of said translation product of (i) a cystatin C gene or (ii) a polymorphic variant of a cystatin C gene relative to a reference value representing a known health status; or a level, or activity, or both said level and said activity, of said transcription product and/or said translation product similar or equal to a reference value representing a known disease status indicates a diagnosis, or prognosis, or increased risk of developing Alzheimer's disease

25. The kit according to claim 23 and/or 24, wherein a presence of a polymorphism in leucin 68 codon of a human cystatin C gene leading to a loss of *Alu* I restriction site does not indicate diagnosis or prognosis of Alzheimer's disease in said subject.

26. The kit according to one of claims 23 to 25, further comprising reagents to assess a function or dysfunction of said subject's kidneys.

27. The kit according to one of claims 23 to 26, wherein said translation product of (i) a cystatin C gene or (ii) a polymorphic variant of a cystatin C gene is determined in its monomer form.

28. A method of treating or preventing Alzheimer's disease in a subject comprising administering to said subject in a therapeutically effective amount an agent or agents which directly or indirectly affect an activity, or level, or both said activity and level, of

- a cystatin C gene or a polymorphic variant of a cystatin C gene, and/or
- a transcription product of (i) a cystatin C gene or (ii) a polymorphic variant of a cystatin C gene, and/or
- a translation product of (i) a cystatin C gene or (ii) a polymorphic variant of a cystatin C gene.

29. The method according to claim 28, wherein said agents are cathepsin derivatives or cystatin C analoga.

30. The method according to one of claims 28 and/or 29, wherein per se known methods of gene therapy and/or antisense nucleic acid technology are applied to administer said agent or agents.

31. The method according to at least one of claims 28 to 30 comprising grafting donor cells into the central nervous system, preferably the brain, of said subject, said subject or donor cells preferably treated so as to minimize or reduce graft rejection, wherein said donor cells are genetically modified by insertion of at least one transgene encoding said agent or agents.

32. An agent which directly or indirectly affects an activity, or level, or both said activity and level, of at least one substance which is selected from the group consisting of a cystatin C gene, a polymorphic variant of a cystatin C gene, a transcription product of a cystatin C gene, a transcription product

of a polymorphic variant of a cystatin C gene, a translation product of a cystatin C gene and a translation product of a polymorphic variant of a cystatin C gene.

33. A medicament comprising an agent according to claim 32.

34. An agent which directly or indirectly affects an activity, or level, or both said activity and level, of at least one substance which is selected from the group consisting of a cystatin C gene, a polymorphic variant of a cystatin C gene, a transcription product of a cystatin C gene, a transcription product of a polymorphic variant of a cystatin C gene, a translation product of a cystatin C gene and a translation product of a polymorphic variant of a cystatin C gene for treating or preventing a disease.

35. Use of an agent which directly or indirectly affects an activity, or level, or both said activity and level, of at least one substance which is selected from the group consisting of a cystatin C gene, a polymorphic variant of a cystatin C gene, a transcription product of a cystatin C gene, a transcription product of a polymorphic variant of a cystatin C gene, a translation product of a cystatin C gene and a translation product of a polymorphic variant of a cystatin C gene for a preparation of a medicament for treating or preventing a neurodegenerative disease, in particular Alzheimer's disease.

36. A method for identifying an agent that directly or indirectly affects an activity, or level, or both said activity and level, of at least one substance which is selected from the group consisting of a cystatin C gene, a polymorphic variant of a cystatin C gene, a transcription product of a cystatin C gene, a transcription product of a polymorphic variant of a cystatin C gene, a translation product of a cystatin C gene and a translation product of a polymorphic variant of a cystatin C gene, comprising the steps of:

(a) providing a sample comprising at least one substance which is selected from the group consisting of a cystatin C gene, a polymorphic variant of a cystatin C gene, a transcription product of a cystatin C gene, a transcription product of a polymorphic variant of a cystatin C gene, a translation product of a cystatin C gene and a translation product of a polymorphic variant of a cystatin C gene;

(b) contacting said sample with at least one agent;

(c) comparing an activity, or level, or both said activity and level, of at least one of said substances before and after said contacting.